

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

Claim 1. (Currently amended) A neovascularization inhibitor comprising the following polypeptide (a) or (b) as an active ingredient:

(a) a polypeptide having the amino acid sequence PyrGlu³² [[~]]to Val⁴⁷⁸ of human hepatocyte growth factor (HGF); or

(b) a polypeptide having an amino acid sequence derived from the amino acid sequence of (a) by the deletion, substitution or addition of one or several~~more~~ amino acids and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF;

wherein the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF.

Claim 2. (Currently amended) A neovascularization inhibitor comprising the following polypeptide (a) or (b) as an active ingredient:

(a) a polypeptide having the amino acid sequence PyrGlu³² [[~]]to Val⁴⁷⁸ of human hepatocyte growth factor (HGF); or

(b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or several~~more~~ amino acids, and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF

and inhibitory action against the growth of vascular endothelial cells induced by bFGF and/or VEGF;

wherein the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF.

Claim 3. (Currently amended) ~~A~~The neovascularization inhibitor as set forth in claim 1 or 2, wherein said polypeptide has at least one hairpin domain and 4 Kringle domains.

Claim 4. (Currently amended) ~~A~~The neovascularization inhibitor as set forth in claim 1 or 2, wherein said polypeptide is ~~one~~-obtainable by elastase digestion of human hepatocyte growth factor harboring a deletion of amino acids 162-166.

Claim 5. (Canceled)

Claim 6. (Currently amended) A neovascularization inhibitor composition comprising the polypeptide defined by SEQ ID NO:2 and a pharmaceutically acceptable carrier.

Claims 7-11. (Canceled)

Claim 12. (Currently amended) A method of inhibiting neovascularization which comprises administering to a subject in need of such treatment a neovascularization inhibitor

composition comprising the following polypeptide (a) or (b) and a pharmaceutically acceptable carrier:

- (a) a polypeptide having the amino acid sequence PyrGlu³² [[~]]to Val⁴⁷⁸ of human hepatocyte growth factor (HGF); or
- (b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or several~~more~~ amino acids and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF;
wherein the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF.

Claim 13. (Currently amended) A method of inhibiting neovascularization which comprises administering to a subject in need of such treatment a neovascularization inhibitor composition comprising the following polypeptide (a) or (b) and a pharmaceutically acceptable carrier:

- (a) a polypeptide having the amino acid sequence PyrGlu³² [[~]] Val⁴⁷⁸ of human hepatocyte growth factor (HGF); or
- (b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or several~~more~~ amino acids, and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF and inhibitory action against the growth of vascular endothelial cells induced by bFGF and/or VEGF;

wherein the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF.

Claim 14. (Currently amended) A method for ~~treating~~prophylaxis or therapy of a disease associated with abnormal angiopoiesis which comprises administering, to a subject in need of such treatment, a neovascularization inhibitor composition comprising the following polypeptide (a) or (b) and a pharmaceutically acceptable carrier:

(a) a polypeptide having the amino acid sequence PyrGlu³² [[~]]to Val⁴⁷⁸ of human hepatocyte growth factor (HGF); or

(b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or ~~several~~more amino acids and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF ~~to a subject in whom a prophylactic or therapeutic treatment for said disease is indicated;~~

wherein the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF.

Claim 15. (Currently amended) A method for ~~treating~~prophylaxis or therapy of a disease associated with abnormal angiopoiesis which comprises administering, to a subject in need of such treatment, a neovascularization inhibitor composition comprising the following polypeptide (a) or (b) and a pharmaceutically acceptable carrier:

(a) a polypeptide having the amino acid sequence PyrGlu³² [[~]]to Val⁴⁷⁸ of human hepatocyte growth factor (HGF); or

(b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or several~~more~~ amino acids, and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF and inhibitory action against the growth of vascular endothelial cells induced by bFGF and/or VEGF;

wherein the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF~~to a subject in whom a prophylactic or therapeutic treatment for said disease is indicated.~~

Claim 16. (Withdrawn-Currently amended) The method offer prophylaxis or therapy~~as set forth in~~ claim 14 or 15, wherein said disease is any disease selected from the group consisting of rheumatoid arthritis, psoriasis, Osler-Webber syndrome, myocardial angiopoiesis, telangiectasia, hemophilic joint, angiogenic diseases of the eye, angiofibroma, benign tumors, wound granulation, enteric adhesion, Crohn's disease, atherosclerosis, scleroderma and overcicatrization.

Claims 17-18. (Cancelled)

Claim 19. (Previously Presented) A polypeptide having an amino acid sequence defined by SEQ ID NO:2.

Claim 20. (Currently amended) A pharmaceutical composition ~~comprising~~containing, as an active ingredient, ~~the~~ polypeptide having ~~the~~ amino acid sequence ~~of defined by SEQ ID NO:2 as an active ingredient~~.

Claims 21-27. (Canceled)

Claim 28. (Currently amended) A method for ~~treating~~prophylaxis or therapy of a solid cancer and/or cancer metastasis, which comprises administering to a subject in need of such treatment a pharmaceutical composition containing the following polypeptide (a) or (b):

(a) a polypeptide having the amino acid sequence PyrGlu³² ~ Val⁴⁷⁸ of human hepatocyte~~hepatoeyte~~ growth factor (HGF); or

(b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or several~~more~~ amino acids;

wherein the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF.

Claim 29. (Currently amended) A method for ~~treating~~prophylaxis or therapy of a solid cancer and/or cancer metastasis, which comprises administering to a subject in need of such

treatment a pharmaceutical composition containing the polypeptide having an amino sequence defined by ~~SEQ ID NO:1~~ or SEQ ID NO:2.

Claim 30. (Currently amended) A ~~The method for prophylaxis or therapy~~ as claimed in Claim 28 or Claim 29, wherein said subject has a cancer ~~of solid cancer or cancer of cancer metastasis is~~ lung cancer or mammary cancer.

Claim 31. (Currently amended) A method for ~~inhibiting~~inhibition of tumor growth or metastasis, which comprises administering to a subject in need of such treatment a pharmaceutical composition containing the following polypeptide (a) or (b):

(a) a polypeptide having the amino acid sequence PyrGlu³² ~~[[~]]~~to Val⁴⁷⁸ of human hepatocyte~~heaptocyte~~ growth factor (HGF); or

(b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or ~~several~~more amino acids;

wherein the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF.

Claim 32. (Currently amended) A method for ~~inhibiting~~inhibition of tumor growth ~~or~~and metastasis, which comprises administering to a subject in need of such treatment a

pharmaceutical composition containing the polypeptide having an amino acid sequence defined by ~~SEQ ID NO:1 or~~ SEQ ID NO:2.

Claim 33. (Currently amended) A ~~The~~ method for inhibiting tumor growth or metastasis prophylaxis or therapy as claimed in Claim 31 or Claim 32, wherein the subject ~~has~~ tumor is lung cancer or mammary cancer.

Claim 34. (Currently amended) A method for treating a disease ~~prophylaxis or therapy of diseases~~ arising from vascular hyperplasia and/or ~~diseases~~ caused by an excessive or abnormal stimulation of the endothelial cells, which comprises administering to a subject in need of such treatment a pharmaceutical composition containing the following polypeptide (a) or (b):

(a) a polypeptide having the amino acid sequence PyrGlu³² ~~[[~]]~~ to Val⁴⁷⁸ of human ~~hepatocyte~~ ~~hepatoeye~~ growth factor (HGF); or

(b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or ~~several~~ more amino acids;

wherein the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF.

Claim 35. (Currently amended) A method for treating a disease ~~prophylaxis or therapy of diseases~~ arising from vascular hyperplasia or/and ~~diseases~~ caused by an excessive or

abnormal stimulation of the endothelial cells, which comprises administering to a subject in need of such treatment a pharmaceutical composition containing the polypeptide having an amino acid sequence defined by ~~SEQ ID NO:1~~ or SEQ ID NO:2.

Claim 36. (Currently amended) A ~~The method~~ offer prophylaxis or therapy as ~~claimed in~~ Claim 34 or Claim 35, wherein said disease is a disease selected from the group consisting of rheumatoid arthritis, psoriasis, Osler Webber syndrome, myocardial angiopoiesis, telangiectasia, hemophilic joint, angiogenic diseases of the eyes, angiofibroma, benign tumors, hematopoietic malignancies, wound granulation, enteric adhesion, Crohn's disease, atherosclerosis, scleroderma and over cicatrization.

Claim 37. (Withdrawn-Currently amended) A method for controlling conception which comprises administering to a subject a pharmaceutical composition comprising~~containing~~ the following polypeptide (a) or (b):

(a) a polypeptide having the amino acid sequence $\text{PyrGlu}^{32} [[\sim]] \text{Val}^{478}$ of human ~~hepatocyte~~hepatocyte growth factor (HGF); or

(b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or several~~more~~ amino acids;

wherein the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human
HGF.